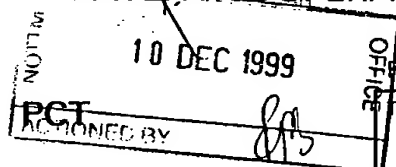


PATENT COOPERATION TREATY



from the INTERNATIONAL BUREAU

NOTICE INFORMING THE APPLICANT OF THE
COMMUNICATION OF THE INTERNATIONAL
APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

to:
BASSETT, Richard
Eric Potter Clarkson
Park View House
58 The Ropewalk
Nottingham NG1 5DD
ROYAUME-UNI

Date of mailing (day/month/year)

02 December 1999 (02.12.99)

Applicant's or agent's file reference

HEWF/P20823PC

IMPORTANT NOTICE

International application No.

PCT/GB99/01600

International filing date (day/month/year)

20 May 1999 (20.05.99)

Priority date (day/month/year)

22 May 1998 (22.05.98)

Applicant

HEWLETT HEALTHCARE LIMITED et al

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:

AU,CN,EP,IL,JP,KP,KR,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,CA,CH,CU,CZ,DE,DK,EA,EE,ES,FI,GB,GD,GE,GH,GM,HR,HU,
ID,IN,IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MD,MG,MK,MN,MW,MX,NO,NZ,OA,PL,PT,RO,RU,SD,
SE,SG,SI,SK,SL,TJ,TM,TR,TT,UA,UG,UZ,VN,YU,ZA,ZW

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on
02 December 1999 (02.12.99) under No. WO 99/60997

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer

J. Zahra

Telephone No. (41-22) 338.83.38

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference
(if desired) (12 characters maximum)

HEWF/P20823PC

Box No. I TITLE OF INVENTION
FORMULATION
Box No. II APPLICANT

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

Hewlett Healthcare Limited
No 1 Mill
The Wharf
Shardlow
Derby DE72 2GH

United Kingdom

☐ This person is also inventor.

Telephone No.

Facsimile No.

Teleprinter No.

State (that is, country) of nationality:

GB

State (that is, country) of residence:

GB

This person is applicant
for the purposes of:
☐ all designated
States

☒ all designated States except
the United States of America

☐ the United States
of America only

☐ the States indicated in
the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

HAWTIN, Brian
Aston Grange
Oaker, Matlock
Derbyshire
United Kingdom

This person is:

☐ applicant only

☒ applicant and inventor

☐ inventor only (If this check-box
is marked, do not fill in below.)

State (that is, country) of nationality:

GB

State (that is, country) of residence:

GB

This person is applicant
for the purposes of:
☐ all designated
States

☐ all designated States except
the United States of America

☒ the United States
of America only

☐ the States indicated in
the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:

☒ agent

☐ common representative

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

BASSETT, Richard
Eric Potter Clarkson
Park View House
58 The Ropewalk
Nottingham NG1 5DD
GB

Telephone No.

(0115) 955 2211

Facsimile No.

(0115) 955 2201

Teleprinter No.

37540 Potter G

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Box No.V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes: at least one must be marked):

Regional Patent

- ☒ AP ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SZ Swaziland, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ EA Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ EP European Patent: AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ OA OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)

National Patent (if other kind of protection or treatment desired, specify on dotted line):

- | | |
|--|--|
| <input checked="" type="checkbox"/> AL Albania | <input checked="" type="checkbox"/> LS Lesotho |
| <input checked="" type="checkbox"/> AM Armenia | <input checked="" type="checkbox"/> LT Lithuania |
| <input checked="" type="checkbox"/> AT Austria | <input checked="" type="checkbox"/> LU Luxembourg |
| <input checked="" type="checkbox"/> AU Australia | <input checked="" type="checkbox"/> LV Latvia |
| <input checked="" type="checkbox"/> AZ Azerbaijan | <input checked="" type="checkbox"/> MD Republic of Moldova |
| <input checked="" type="checkbox"/> BA Bosnia and Herzegovina | <input checked="" type="checkbox"/> MG Madagascar |
| <input checked="" type="checkbox"/> BB Barbados | <input checked="" type="checkbox"/> MK The former Yugoslav Republic of Macedonia |
| <input checked="" type="checkbox"/> BG Bulgaria | <input checked="" type="checkbox"/> MN Mongolia |
| <input checked="" type="checkbox"/> BR Brazil | <input checked="" type="checkbox"/> MW Malawi |
| <input checked="" type="checkbox"/> BY Belarus | <input checked="" type="checkbox"/> MX Mexico |
| <input checked="" type="checkbox"/> CA Canada | <input checked="" type="checkbox"/> NO Norway |
| <input checked="" type="checkbox"/> CH and LI Switzerland and Liechtenstein | <input checked="" type="checkbox"/> NZ New Zealand |
| <input checked="" type="checkbox"/> CN China | <input checked="" type="checkbox"/> PL Poland |
| <input checked="" type="checkbox"/> CU Cuba | <input checked="" type="checkbox"/> PT Portugal |
| <input checked="" type="checkbox"/> CZ Czech Republic | <input checked="" type="checkbox"/> RO Romania |
| <input checked="" type="checkbox"/> DE Germany | <input checked="" type="checkbox"/> RU Russian Federation |
| <input checked="" type="checkbox"/> DK Denmark | <input checked="" type="checkbox"/> SD Sudan |
| <input checked="" type="checkbox"/> EE Estonia | <input checked="" type="checkbox"/> SE Sweden |
| <input checked="" type="checkbox"/> ES Spain | <input checked="" type="checkbox"/> SG Singapore |
| <input checked="" type="checkbox"/> FI Finland | <input checked="" type="checkbox"/> SI Slovenia |
| <input checked="" type="checkbox"/> GB United Kingdom | <input checked="" type="checkbox"/> SK Slovakia |
| <input checked="" type="checkbox"/> GD Grenada | <input checked="" type="checkbox"/> SL Sierra Leone |
| <input checked="" type="checkbox"/> GE Georgia | <input checked="" type="checkbox"/> TJ Tajikistan |
| <input checked="" type="checkbox"/> GH Ghana | <input checked="" type="checkbox"/> TM Turkmenistan |
| <input checked="" type="checkbox"/> GM Gambia | <input checked="" type="checkbox"/> TR Turkey |
| <input checked="" type="checkbox"/> HR Croatia | <input checked="" type="checkbox"/> TT Trinidad and Tobago |
| <input checked="" type="checkbox"/> HU Hungary | <input checked="" type="checkbox"/> UA Ukraine |
| <input checked="" type="checkbox"/> ID Indonesia | <input checked="" type="checkbox"/> UG Uganda |
| <input checked="" type="checkbox"/> IL Israel | <input checked="" type="checkbox"/> US United States of America |
| <input checked="" type="checkbox"/> IN India | <input checked="" type="checkbox"/> UZ Uzbekistan |
| <input checked="" type="checkbox"/> IS Iceland | <input checked="" type="checkbox"/> VN Viet Nam |
| <input checked="" type="checkbox"/> JP Japan | <input checked="" type="checkbox"/> YU Yugoslavia |
| <input checked="" type="checkbox"/> KE Kenya | <input checked="" type="checkbox"/> ZW Zimbabwe |
| <input checked="" type="checkbox"/> KG Kyrgyzstan | |
| <input checked="" type="checkbox"/> KP Democratic People's Republic of Korea | |
| <input checked="" type="checkbox"/> KR Republic of Korea | |
| <input checked="" type="checkbox"/> KZ Kazakhstan | |
| <input checked="" type="checkbox"/> LC Saint Lucia | |
| <input checked="" type="checkbox"/> LK Sri Lanka | |
| <input checked="" type="checkbox"/> LR Liberia | |

Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet:

- ☒ South Africa
- ☐
- ☐

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

Box No. VI PRIORITY CLAIM		<input type="checkbox"/> Further priority claims are indicated in the Supplemental Box.		
Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country	regional application: regional Office	international application: receiving Office
item (1) 22 May 1998 (22.05.98)	9810949.9	GB		
item (2)				
item (3)				

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s): 1.

* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) (if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen: the two-letter code may be used):	Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):
ISA /	Date (day/month/year) Number Country (or regional Office)

Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains the following number of sheets: request : 3 description (excluding sequence listing part) : 42 claims : 5 abstract : 1 drawings : 1 sequence listing part of description : 0 Total number of sheets : 52	This international application is accompanied by the item(s) marked below: 1. <input checked="" type="checkbox"/> fee calculation sheet 2. <input type="checkbox"/> separate signed power of attorney 3. <input checked="" type="checkbox"/> copy of general power of attorney; reference number, if any: 4. <input type="checkbox"/> statement explaining lack of signature 5. <input type="checkbox"/> priority document(s) identified in Box No. VI as item(s): 6. <input type="checkbox"/> translation of international application into (language): 7. <input type="checkbox"/> separate indications concerning deposited microorganism or other biological material 8. <input type="checkbox"/> nucleotide and/or amino acid sequence listing in computer readable form 9. <input checked="" type="checkbox"/> other (specify): <u>Form 23/77</u>
---	--

Figure of the drawings which should accompany the abstract: <u>1</u>	Language of filing of the international application: <u>English</u>
--	---

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).



BASSETT, Richard

For receiving Office use only		2. Drawings: <input type="checkbox"/> received: <input type="checkbox"/> not received:
1. Date of actual receipt of the purported international application:		
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:		
4. Date of timely receipt of the required corrections under PCT Article 11(2):		
5. International Searching Authority (if two or more are competent): <u>ISA /</u>	6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid.	

Date of receipt of the record copy by the International Bureau:	For International Bureau use only
---	-----------------------------------

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:

BASSET, R.
ERIC POTTER CLARKSON
Park View House
58 The Ropewalk
Nottingham NG1 5DD
GRANDE BRETAGNE

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT
(PCT Rule 71.1)Date of mailing
(day/month/year)

13. 07. 00

Applicant's or agent's file reference
HEWF/P20823PC

IMPORTANT NOTIFICATION

International application No.
PCT/GB99/01600International filing date (day/month/year)
20/05/1999Priority date (day/month/year)
22/05/1998Applicant
HEWLETT HEALTHCARE LIMITED

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer

Hebert, W

Tel. +49 89 2399-2152



PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference HEWF/P20823PC	FOR FURTHER ACTION		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB99/01600	International filing date (day/month/year) 20/05/1999	Priority date (day/month/year) 22/05/1998	
International Patent Classification (IPC) or national classification and IPC A61K9/107			
Applicant HEWLETT HEALTHCARE LIMITED			

- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 5 sheets, including this cover sheet.
 - ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 1 sheets.

- This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 24/11/1999	Date of completion of this report 10.07.00
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Economou, D Telephone No. +49 89 2399 8599 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB99/01600

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.)*:

Description, pages:

1-42 as originally filed

Claims, No.:

1-28 as originally filed

29,30 as received on 24/11/1999 with letter of 23/11/1999

Drawings, sheets:

1/1 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
☒ claims Nos. 15,17-18,20-27,30.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/01600

because:

- ☒ the said international application, or the said claims Nos. 15,17-18,20-21,23-24 (see separate sheet, item 2a) relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 22,25-27,30 (see separate sheet, item 1) are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

- ☐ no international search report has been established for the said claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-13, 15, 24 (see separate sheet, item 3)
	No:	Claims	14,16-21,23,28-29 (see separate sheet, item 3)
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-13, 15,24 (see separate sheet, item 3)
Industrial applicability (IA)	Yes:	Claims	15,17-18, 20-21, 23-24 (see separate sheet, items 2a and 2c); 1-14,16,19 and 28-29 (see separate sheet, item 2b)
	No:	Claims	

2. Citations and explanations

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/01600

- 1). According to the PCT Guidelines (see C III, 3.1) the wording of the claims should not leave doubt as to their category. This is obviously not the case by the wording of claims 22, 25-27 and 30, which defines uses, methods and compositions.
- 2).
 - a). Claims 15,17-18, 20-21,23-24 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).
 - b). The subject-matter of claims 1-14, 16, 19 and 28-29 fulfils the requirements of industrial applicability.
 - c). For the assessment of the present claims 15,17-18, 20-21 and 23-24 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.
- 3). **D1** (=ARIYANAYAGAM M. ET AL.: "Topical sodium cromoglycate in the management of atopic eczema-a controlled trial" BR.J.DERMATOL., vol. 112, no. 3, March 1985 (1985-03), pages 343-348, UK,; cited in the application) relates to a topical composition comprising sodium cromoglycate administered for the treatment of chronic atopic eczema (see abstract; see page 344, last paragraph). An O/W cream formulation comprising 4% SCG is disclosed on page 343, penultimate paragraph). This citation takes away the novelty of claims 14,17-21,23 and 28-29 since it discloses all the technical features of the said claims.

D2 (=EP-A-0 189 861) relates to a percutaneous or transdermal absorption accelerator for ionic water soluble medicines or pharmaceutically active agents and more specifically, to the percutaneous absorption acceleration of ionic water-soluble medicines including cationic and anionic water-soluble medicines by incorporating ionic oil-soluble substances and their salts, amphoteric surfactants,

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/01600

and/or nonionic substances into transdermal therapeutic preparations containing the ionic water-soluble medicines (see page 1, lines 3-12). Amphoteric surfactants and nonionic substances are disclosed 5, lines 1-2 as absorption accelerators. Disodium cromoglycate, dexamethason sodium phosphate and betamethason disodium phosphate are explicitly disclosed on page 6, second paragraph as anionic water-soluble active agents. Amphoteric surfactants are disclosed from page 8, line 14 to page 9, line 20. Polyoxyethylene cetyl ether is disclosed as a preferable nonionic substance on page 10, lines 20 and 23-24.

Example 142 discloses an ointment comprising 2-undecyl-N-carboxymethyl-N-hydroxyethyl imidazolium betaine as the amphoteric surfactant, polyoxyethylene lauryl ether and salbutamol hemisulfate as the polar drug.

Example 147 discloses a poultice comprising 2-undecyl-N-carboxymethyl-N-hydroxyethyl imidazolium betaine as the amphoteric surfactant, polyoxyethylene lauryl ether and diltiazem hydrochloride as the polar drug.

Example 157 discloses a poultice comprising 2-undecyl-N-carboxymethyl-N-hydroxyethyl imidazolium betaine as the amphoteric surfactant, polyoxyethylene lauryl ether and disodium cromoglycate as the polar drug.

Claims 1,4,5,10,11 refer to compositions comprising ionic water-soluble drugs (anionic drugs see claims 4 and 5), amphoteric surfactants (see claims 1 and 10) and polyoxyethylene alkyl ethers (see claims 1 and 11).

The subject-matter of claim 16 is not novel since the use of an alkoxylated cetyl alcohol and an amphoteric surfactant for the manufacture of a medicament is already known from **D2** (see analysis of the document above).

The subject-matter of claims 1-13, 15 and 24 is formally novel since a composition comprising an alkoxylated cetyl alcohol an amphoteric surfactant and a polar drug is not explicitly mentioned in **D2**.

However, the use of an alkoxylated cetyl alcohol as an equivalent to polyoxyethylene lauryl ether is obvious fro the skilled person and hence an inventive step cannot be acknowledged for the subject-matter of claims 1-13, 15 and 24 since the system polyoxyethylene alkyl ether/amphoteric surfactant as a vehicle allowing adequate penetration of polar drugs is obvious from **D2** (see above).

24-11-1999

99922371.2 - GB99/01600

Replacement

CLMSPAMD

24.11.99
47

29. A composition or emulsion according to any one of claims 1 to 14 for use in medicine.

- 5 30. A composition, method or use according to any of claims 1 to 13 or 15 to 29 (when dependent on claims 1 to 13), wherein the alkoxylated cetyl alcohol is polypropoxylated cetyl alcohol.

AMENDED SHEET

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

ERIC POTTER CLARKSON
Attn. BASSET, R.
Park View House
58 The Ropewalk
Nottingham NG1 5DD
UNITED KINGDOM

COMUS

PARTNER

STM
N

17 SEP 1999

ACTIONED BY

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing
(day/month/year)

14/09/1999

Applicant's or agent's file reference

HEWF/P20823PC

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/GB 99/01600

International filing date
(day/month/year)

20/05/1999

Applicant

HEWLETT HEALTHCARE LIMITED

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.


4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority

 European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Wolfgang Borinski

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference HEWF/P20823PC	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 99/01600	International filing date (day/month/year) 20/05/1999	(Earliest) Priority Date (day/month/year) 22/05/1998
Applicant HEWLETT HEALTHCARE LIMITED		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (see Box II).

4. With regard to the title,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

PHARMACEUTICAL COMPOSITIONS COMPRISING AN AMPHOTERIC SURFACTANT AN ALKOXYLATED CETYL ALCOHOL AND A POLAR DRUG

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/01600

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 189 861 A (SHOWA DENKO K.K.) 6 August 1986 (1986-08-06) the whole document -----	1-29

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 99/01600

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0189861 A	06-08-1986	JP 61172830 A	04-08-1986
		JP 61254532 A	12-11-1986
		JP 61260026 A	18-11-1986
		JP 61260027 A	18-11-1986
		JP 61268631 A	28-11-1986
		JP 61268632 A	28-11-1986
		JP 62061929 A	18-03-1987
<hr/>			

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/01600

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61K9/107 A61K9/12 A61K31/35

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>ARIYANAYAGAM M. ET AL.: "Topical sodium cromoglycate in the management of atopic eczema-a controlled trial"</p> <p>BR.J.DERMATOL.,</p> <p>vol. 112, no. 3, March 1985 (1985-03),</p> <p>pages 343-348, XP002113842</p> <p>u.k.</p> <p>cited in the application</p> <p>abstract</p> <p>page 343, paragraph 4 - paragraph 5</p> <p>page 344, paragraph 2</p> <p>page 344, last paragraph</p> <p>page 345, paragraph 2</p> <p>page 347, paragraph 3 - page 348,</p> <p>paragraph 2</p> <p>---</p> <p>-/--</p>	<p>14,</p> <p>17-21,29</p>

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

31 August 1999

Date of mailing of the international search report

14/09/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2

NL - 2280 HV Rijswijk

Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,

Fax: (+31-70) 340-3016

Authorized officer

Economou, D

The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are competent, with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line below:

CHAPTER II

under Article 31 of the Patent Cooperation Treaty:
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty and hereby elects all eligible States (except where otherwise indicated).

See Notes to the demand form

Sheet No. 2.

International application No.
GB99/01600**Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE**The following person is ☒ agent ☐ common representativeand ☒ has been appointed earlier and represents the applicant(s) also for international preliminary examination.☐ is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

BASSETT, Richard
Eric Potter Clarkson
Park View House
58 The Ropewalk
Nottingham NG1 5DD
United Kingdom

Telephone No.:

(0115) 955 2211

Facsimile No.:

(0115) 955 2201

Teleprinter No.:

37540 Potter G

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.**Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION****Statement concerning amendments:***

1. The applicant wishes the international preliminary examination to start on the basis of:

☐ the international application as originally filedthe description ☒ as originally filed☐ as amended under Article 34the claims ☐ as originally filed☒ as amended under Article 19 (together with any accompanying statement)☐ as amended under Article 34the drawings ☒ as originally filed☐ as amended under Article 342. ☐ The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.3. ☐ The applicant wishes the start of the international preliminary examination to be postponed until the expiration of 20 months from the priority date unless the International Preliminary Examining Authority receives a copy of any amendments made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69.1(d)). *(This check-box may be marked only where the time limit under Article 19 has not yet expired.)*

* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

Language for the purposes of international preliminary examination: English☒ which is the language in which the international application was filed.☐ which is the language of a translation furnished for the purposes of international search.☐ which is the language of publication of the international application.☐ which is the language of the translation (to be) furnished for the purposes of international preliminary examination.**Box No. V ELECTION OF STATES**

The applicant hereby elects all eligible States (that is, all States which have been designated and which are bound by Chapter II of the PCT)

excluding the following States which the applicant wishes not to elect:

Sheet No. 3

International application No.
GB99/01600

Box No. VI CHECK LIST

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:

- | | | |
|--|---|----------|
| 1. translation of international application | : | sheets |
| 2. amendments under Article 34 | : | sheets |
| 3. copy (or, where required, translation) of amendments under Article 19 | : | 1 sheets |
| 4. copy (or, where required, translation) of statement under Article 19 | : | sheets |
| 5. letter | : | sheets |
| 6. other (specify) | : | sheets |

For International Preliminary Examining Authority use only

received	not received
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>

The demand is also accompanied by the item(s) marked below:

- | | |
|---|---|
| 1. <input checked="" type="checkbox"/> fee calculation sheet | 4. <input type="checkbox"/> statement explaining lack of signature |
| 2. <input type="checkbox"/> separate signed power of attorney | 5. <input type="checkbox"/> nucleotide and/or amino acid sequence listing in computer readable form |
| 3. <input checked="" type="checkbox"/> copy of general power of attorney; reference number, if any: | 6. <input type="checkbox"/> other (specify): |

Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).



Richard Bassett

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:

2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):

3. ☐ The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply.

☐ The applicant has been informed accordingly.

4. ☐ The date of receipt of the demand is WITHIN the period of 19 months from the priority date as extended by virtue of Rule 80.5.

5. ☐ Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82.

For International Bureau use only

Demand received from IPEA on:

CHAPTER II

PCT

FEE CALCULATION SHEET

Annex to the Demand for international preliminary examination

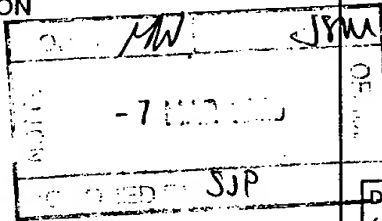
<p>International application No. GB99/01600</p> <p>Applicant's or agent's file reference HEWF/P20823PC</p> <p>Applicant Hewlett Healthcare Limited, et al</p>	<p>For International Preliminary Examining Authority use only</p> <p>Date stamp of the IPEA</p>								
<p>Calculation of prescribed fees</p> <p>1. Preliminary examination fee 1533 Euro P</p> <p>2. Handling fee (<i>Applicants from certain States are entitled to a reduction of 75% of the handling fee. Where the applicant is (or all applicants are) so entitled, the amount to be entered at H is 25% of the handling fee.</i>) 148 Euro H</p> <p>3. Total of prescribed fees Add the amounts entered at P and H and enter total in the TOTAL box.....</p> <div style="border: 1px solid black; padding: 5px; width: fit-content; margin-left: 350px;"> <p>1681 Euro</p> <p>TOTAL</p> </div>									
<p>Mode of Payment</p> <table style="width: 100%;"> <tr> <td><input type="checkbox"/> authorization to charge deposit account with the IPEA (see below)</td> <td><input type="checkbox"/> cash</td> </tr> <tr> <td><input type="checkbox"/> cheque</td> <td><input type="checkbox"/> revenue stamps</td> </tr> <tr> <td><input type="checkbox"/> postal money order</td> <td><input type="checkbox"/> coupons</td> </tr> <tr> <td><input type="checkbox"/> bank draft</td> <td><input type="checkbox"/> other (specify):</td> </tr> </table>		<input type="checkbox"/> authorization to charge deposit account with the IPEA (see below)	<input type="checkbox"/> cash	<input type="checkbox"/> cheque	<input type="checkbox"/> revenue stamps	<input type="checkbox"/> postal money order	<input type="checkbox"/> coupons	<input type="checkbox"/> bank draft	<input type="checkbox"/> other (specify):
<input type="checkbox"/> authorization to charge deposit account with the IPEA (see below)	<input type="checkbox"/> cash								
<input type="checkbox"/> cheque	<input type="checkbox"/> revenue stamps								
<input type="checkbox"/> postal money order	<input type="checkbox"/> coupons								
<input type="checkbox"/> bank draft	<input type="checkbox"/> other (specify):								
<p>Deposit Account Authorization (<i>this mode of payment may not be available at all IPEAs</i>)</p> <p>The IPEA/ _____ <input type="checkbox"/> is hereby authorized to charge the total fees indicated above to my deposit account.</p> <p><input type="checkbox"/> (<i>this check-box may be marked only if the conditions for deposit accounts of the IPEA so permit</i>) is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.</p>									
<p>Deposit Account Number _____</p>	<p>Date (day/month/year) _____</p>								
<p>Signature _____</p>									

PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

BASSET, R.
ERIC POTTER CLARKSON
Park View House
58 The Ropewalk
Nottingham NG1 5DD
GRANDE BRETAGNE



PCT

WRITTEN OPINION

(PCT Rule 66)

Date of mailing (day/month/year)		03.03.2000
Applicant's or agent's file reference HEWF/P20823PC		REPLY DUE within 3 month(s) from the above date of mailing
International application No. PCT/GB99/01600	International filing date (day/month/year) 20/05/1999	Priority date (day/month/year) 22/05/1998
International Patent Classification (IPC) or both national classification and IPC A61K9/107		
Applicant HEWLETT HEALTHCARE LIMITED		

- This written opinion is the **first** drawn up by this International Preliminary Examining Authority.
- This opinion contains indications relating to the following items:
 - ☒ Basis of the opinion
 - ☐ Priority
 - ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - ☐ Lack of unity of invention
 - ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - ☐ Certain document cited
 - ☐ Certain defects in the international application
 - ☐ Certain observations on the international application
- The applicant is hereby **invited to reply** to this opinion.


When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.
- The final date by which the international preliminary examination report must be established according to Rule 69.2 is: **22/09/2000**.

Name and mailing address of the international preliminary examining authority:

 European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer / Examiner

Economou, D

Formalities officer (incl. extension of time limits)

Hebert, W

Telephone No. +49 89 2399 2152



I. Basis of the opinion

1. This opinion has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"*).

Description, pages:

1-42 as originally filed

Claims, No.:

1-28 as originally filed

29,30 as received on 24/11/1999 with letter of 23/11/1999

Drawings, sheets:

1/1 as received on 06/07/1999 with letter of 05/07/1999

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

- ☐ the entire international application,
☒ claims Nos. 15,17-18,20-27,30,

because:

WRITTEN OPINION

International application No. PCT/GB99/01600

- ☒ the said international application, or the said claims Nos. 15,17-18,20-21,23-24 (see separate sheet, item 2a) relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 22,25-27,30 (see separate sheet, item 1) are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

- ☐ no international search report has been established for the said claims Nos. .

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	14,16-21,23,28-29 (NO; see separate sheet, item 3); 1-13,15,24 (YES; see separate sheet, item 3)
Inventive step (IS)	Claims	1-13,15,24 (NO; see separate sheet, item 3)
Industrial applicability (IA)	Claims	15,17-18,20-21,23-24 (see separate sheet, items 2a and 2c); 1-14,16,19 and 28-29 (YES; see separate sheet, item 2b)

2. Citations and explanations

see separate sheet

- 1). According to the PCT Guidelines (see C III, 3.1) the wording of the claims should not leave doubt as to their category. This is obviously not the case by the wording of claims 22, 25-27 and 30, which defines uses, methods and compositions.
- 2).
 - a). Claims 15,17-18, 20-21,23-24 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).
 - b). The subject-matter of claims 1-14, 16, 19 and 28-29 fulfils the requirements of industrial applicability.
 - c). For the assessment of the present claims 15,17-18, 20-21 and 23-24 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.
- 3). **D1** (=ARIYANAYAGAM M. ET AL.: "Topical sodium cromoglycate in the management of atopic eczema-a controlled trial" BR.J.DERMATOL., vol. 112, no. 3, March 1985 (1985-03), pages 343-348, UK,; cited in the application) relates to a topical composition comprising sodium cromoglycate administered for the treatment of chronic atopic eczema (see abstract; see page 344, last paragraph). An O/W cream formulation comprising 4% SCG is disclosed on page 343, penultimate paragraph). This citation takes away the novelty of claims 14,17-21,23 and 28-29 since it discloses all the technical features of the said claims.

D2 (=EP-A-0 189 861) relates to a percutaneous or transdermal absorption accelerator for ionic water soluble medicines or pharmaceutically active agents and more specifically, to the percutaneous absorption acceleration of ionic water-soluble medicines including cationic and anionic water-soluble medicines by incorporating ionic oil-soluble substances and their salts, amphoteric surfactants,

and/or nonionic substances into transdermal therapeutic preparations containing the ionic water-soluble medicines (see page 1, lines 3-12). Amphoteric surfactants and nonionic substances are disclosed 5, lines 1-2 as absorption accelerators. Disodium cromoglycate, dexamethason sodium phosphate and betamethason disodium phosphate are explicitly disclosed on page 6, second paragraph as anionic water-soluble active agents. Amphoteric surfactants are disclosed from page 8, line 14 to page 9, line 20. Polyoxyethylene cetyl ether is disclosed as a preferable nonionic substance on page 10, lines 20 and 23-24.

Example 142 discloses an ointment comprising 2-undecyl-N-carboxymethyl-N-hydroxyethyl imidazolium betaine as the amphoteric surfactant, polyoxyethylene lauryl ether and salbutamol hemisulfate as the polar drug.

Example 147 discloses a poultice comprising 2-undecyl-N-carboxymethyl-N-hydroxyethyl imidazolium betaine as the amphoteric surfactant, polyoxyethylene lauryl ether and diltiazem hydrochloride as the polar drug.

Example 157 discloses a poultice comprising 2-undecyl-N-carboxymethyl-N-hydroxyethyl imidazolium betaine as the amphoteric surfactant, polyoxyethylene lauryl ether and disodium cromoglycate as the polar drug.

Claims 1,4,5,10,11 refer to compositions comprising ionic water-soluble drugs (anionic drugs see claims 4 and 5), amphoteric surfactants (see claims 1 and 10) and polyoxyethylene alkyl ethers (see claims 1 and 11).

The subject-matter of claim 16 is not novel since the use of an alkoxyated cetyl alcohol and an amphoteric surfactant for the manufacture of a medicament is already known from **D2** (see analysis of the document above).

The subject-matter of claims 1-13, 15 and 24 is formally novel since a composition comprising an alkoxyated cetyl alcohol an amphoteric surfactant and a polar drug is not explicitly mentioned in **D2**.

However, the use of an alkoxyated cetyl alcohol as an equivalent to polyoxyethylene lauryl ether is obvious fro the skilled person and hence an inventive step cannot be acknowledged for the subject-matter of claims 1-13, 15 and 24 since the system polyoxyethylene alkyl ether/amphoteric surfactant as a vehicle allowing adequate penetration of polar drugs is obvious from **D2** (see above).

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference HEWF/P20823PC		FOR FURTHER ACTION		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB99/01600	International filing date (day/month/year) 20/05/1999	Priority date (day/month/year) 22/05/1998		
International Patent Classification (IPC) or national classification and IPC A61K9/107		<div style="border: 1px solid black; padding: 2px;"> <div style="border-bottom: 1px solid black; margin-bottom: 2px;"> <div style="float: left;">CLASS</div> <div style="float: right;">PCT</div> </div> </div>		
Applicant HEWLETT HEALTHCARE LIMITED				

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.


2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 24/11/1999	Date of completion of this report 13.07.00
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Economou, D Telephone No. +49 89 2399 8599



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/01600

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-42 as originally filed

Claims, No.:

1-28 as originally filed

29,30 as received on 24/11/1999 with letter of 23/11/1999

Drawings, sheets:

1/1 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
☒ claims Nos. 15,17-18,20-27,30.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/01600

because:

- ☒ the said international application, or the said claims Nos. 15,17-18,20-21,23-24 (see separate sheet, item 2a) relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 22,25-27,30 (see separate sheet, item 1) are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

- ☐ no international search report has been established for the said claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-13, 15, 24 (see separate sheet, item 3)
	No:	Claims	14,16-21,23,28-29 (see separate sheet, item 3)
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-13, 15,24 (see separate sheet, item 3)
Industrial applicability (IA)	Yes:	Claims	15,17-18, 20-21, 23-24 (see separate sheet, items 2a and 2c); 1-14,16,19 and 28-29 (see separate sheet, item 2b)
	No:	Claims	

2. Citations and explanations

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/01600

- 1). According to the PCT Guidelines (see C III, 3.1) the wording of the claims should not leave doubt as to their category. This is obviously not the case by the wording of claims 22, 25-27 and 30, which defines uses, methods and compositions.
- 2).
 - a). Claims 15,17-18, 20-21,23-24 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).
 - b). The subject-matter of claims 1-14, 16, 19 and 28-29 fulfils the requirements of industrial applicability.
 - c). For the assessment of the present claims 15,17-18, 20-21 and 23-24 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.
- 3). **D1** (=ARIYANAYAGAM M. ET AL.: "Topical sodium cromoglycate in the management of atopic eczema-a controlled trial" BR.J.DERMATOL., vol. 112, no. 3, March 1985 (1985-03), pages 343-348, UK,; cited in the application) relates to a topical composition comprising sodium cromoglycate administered for the treatment of chronic atopic eczema (see abstract; see page 344, last paragraph). An O/W cream formulation comprising 4% SCG is disclosed on page 343, penultimate paragraph). This citation takes away the novelty of claims 14,17-21,23 and 28-29 since it discloses all the technical features of the said claims.

D2 (=EP-A-0 189 861) relates to a percutaneous or transdermal absorption accelerator for ionic water soluble medicines or pharmaceutically active agents and more specifically, to the percutaneous absorption acceleration of ionic water-soluble medicines including cationic and anionic water-soluble medicines by incorporating ionic oil-soluble substances and their salts, amphoteric surfactants,

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/01600

and/or nonionic substances into transdermal therapeutic preparations containing the ionic water-soluble medicines (see page 1, lines 3-12). Amphoteric surfactants and nonionic substances are disclosed 5, lines 1-2 as absorption accelerators. Disodium cromoglycate, dexamethason sodium phosphate and betamethason disodium phosphate are explicitly disclosed on page 6, second paragraph as anionic water-soluble active agents. Amphoteric surfactants are disclosed from page 8, line 14 to page 9, line 20. Polyoxyethylene cetyl ether is disclosed as a preferable nonionic substance on page 10, lines 20 and 23-24.

Example 142 discloses an ointment comprising 2-undecyl-N-carboxymethyl-N-hydroxyethyl imidazolium betaine as the amphoteric surfactant, polyoxyethylene lauryl ether and salbutamol hemisulfate as the polar drug.

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Example 157 discloses a poultice comprising 2-undecyl-N-carboxymethyl-N-hydroxyethyl imidazolium betaine as the amphoteric surfactant, polyoxyethylene lauryl ether and disodium cromoglycate as the polar drug.

Claims 1,4,5,10,11 refer to compositions comprising ionic water-soluble drugs (anionic drugs see claims 4 and 5), amphoteric surfactants (see claims 1 and 10) and polyoxyethylene alkyl ethers (see claims 1 and 11).

The subject-matter of claim 16 is not novel since the use of an alkoxyated cetyl alcohol and an amphoteric surfactant for the manufacture of a medicament is already known from **D2** (see analysis of the document above).

The subject-matter of claims 1-13, 15 and 24 is formally novel since a composition comprising an alkoxyated cetyl alcohol an amphoteric surfactant and a polar drug is not explicitly mentioned in **D2**.

However, the use of an alkoxyated cetyl alcohol as an equivalent to polyoxyethylene lauryl ether is obvious fro the skilled person and hence an inventive step cannot be acknowledged for the subject-matter of claims 1-13, 15 and 24 since the system polyoxyethylene alkyl ether/amphoteric surfactant as a vehicle allowing adequate penetration of polar drugs is obvious from **D2** (see above).

AMENDED CLAIMS

[received by the International Bureau on 25 October 1999 (25.10.99);
new claim 30 added; remaining claims unchanged (1 page)]

- 5 30. A composition, method or use according to any of claims 1 to 13 or 15 to 29 (when dependent on claims 1 to 13), wherein the alkoxyated cetyl alcohol is polypropoxylated cetyl alcohol.

REPLACED BY
ART 34 A/2001

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29. A composition or emulsion according to any one of claims 1 to 14 for use in medicine.

REPLACED BY
ART 81/1997

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference HEWF/P20823PC	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 99/ 01600	International filing date (day/month/year) 20/05/1999	(Earliest) Priority Date (day/month/year) 22/05/1998
Applicant HEWLETT HEALTHCARE LIMITED		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

PHARMACEUTICAL COMPOSITIONS COMPRISING AN AMPHOTERIC SURFACTANT AN ALKOXYLATED CETYL ALCOHOL AND A POLAR DRUG

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/01600

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61K9/107 A61K9/12 A61K31/35

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>ARIYANAYAGAM M. ET AL.: "Topical sodium cromoglycate in the management of atopic eczema-a controlled trial"</p> <p>BR.J.DERMATOL.,</p> <p>vol. 112, no. 3, March 1985 (1985-03),</p> <p>pages 343-348, XP002113842</p> <p>u.k.</p> <p>cited in the application</p> <p>abstract</p> <p>page 343, paragraph 4 - paragraph 5</p> <p>page 344, paragraph 2</p> <p>page 344, last paragraph</p> <p>page 345, paragraph 2</p> <p>page 347, paragraph 3 - page 348,</p> <p>paragraph 2</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p>	<p>14,</p> <p>17-21,29</p>



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

31 August 1999

Date of mailing of the international search report

14/09/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2

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Authorized officer

Economou, D

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/01600

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>EP 0 189 861 A (SHOWA DENKO K.K.) 6 August 1986 (1986-08-06) the whole document -----</p>	1-29

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 99/01600

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0189861 A	06-08-1986	JP 61172830 A	04-08-1986
		JP 61254532 A	12-11-1986
		JP 61260026 A	18-11-1986
		JP 61260027 A	18-11-1986
		JP 61268631 A	28-11-1986
		JP 61268632 A	28-11-1986
		JP 62061929 A	18-03-1987
